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(54) Title: FUNGICIDES		
(57) Abstract		
The invention provides the use in combating fungi of compounds of general formula (I) wherein R ¹ is hydrogen, hydroxy, acyl, acyloxy, optionally substituted amino, R ^a , R ^a Si, R ^a S or R ^a O, where R ^a is optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted aryl or optionally substituted heterocyclic; R ² has the same meaning as R ^a or can be hydrogen; Z is oxygen or sulfur; M is a thiophene ring; and R ³ and R ⁴ , which may be the same or different, have the same meaning as R ^a or can be optionally substituted amino, hydrogen, halogen, cyano, nitro or a group OR ^c or S(O) _m R ^c , where R ^c has the same meaning as R ^a or is hydrogen or acyl and m is 0, 1 or 2; or R ³ and R ⁴ together with the atoms to which they are attached form an optionally substituted carbocyclic or heterocyclic ring; together with tautomers of compounds where R ¹ is hydrogen.	<p style="text-align: center;">(I)</p>	

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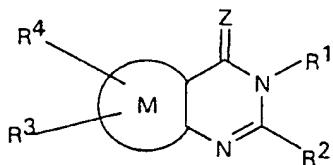
Fungicides

The invention relates to the use of compounds in combating fungi in plants.

- 5 In Bull. Soc. Chim. France, 1970, (10), 3630-6, there are disclosed certain thienopyrimidines. We have discovered that at least one of these compounds has utility in combating fungi.

The invention provides the use in combating fungi of compounds of general

10 formula I



(I)

wherein

R¹ is hydrogen, hydroxy, acyl, acyloxy, optionally substituted amino, R^a, R^a₃Si,

15 R^aS or R^aO, where R^a is optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted aryl or optionally substituted heterocycl;

R² has the same meaning as R^a or can be hydrogen;

Z is oxygen or sulfur;

20 M is a thiophene ring; and

R³ and R⁴, which may be the same or different, have the same meaning as R^a or can be optionally substituted amino, hydrogen, halogen, cyano, nitro or a group OR^C or S(O)_mR^C, where R^C has the same meaning as R^a or is

25 hydrogen or acyl and m is 0, 1 or 2; or R³ and R⁴ together with the atoms to which they are attached form an optionally substituted carbocyclic or heterocyclic ring;

together with tautomers of compounds where R¹ is hydrogen.

Most of the above compounds are novel, and accordingly the invention includes any novel compounds of formula I as defined above.

Any alkyl group present in the molecule is preferably of 1 to 10 carbon atoms,

5 especially of 1 to 7 carbon atoms, and particularly of 1 to 5 carbon atoms.

Any alkenyl or alkynyl group present in the molecule is preferably of 2 to 7 carbon atoms, for example allyl, vinyl or propargyl.

10 Any cycloalkyl, cycloalkenyl or cycloalkynyl group present in the molecule is preferably of 3 to 7 carbon atoms, especially cyclopropyl, cyclopentyl, cyclohexyl or cyclohexenyl.

Substituents, when present on any alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl
15 cycloalkynyl moiety may for example be halogen, cyano, optionally substituted alkoxy, optionally substituted alkylthio, mercapto, hydroxy, nitro, optionally substituted amino, acyl, acyloxy, acylthio, optionally substituted phenyl, optionally substituted heterocycl, optionally substituted phenylthio, optionally substituted phenoxy, optionally substituted heterocyclyoxy, optionally substituted heterocyclthio.

20 Cycloalkyl, cycloalkenyl, cycloalkynyl groups may also be substituted by optionally substituted alkyl, alkynyl or alkenyl and vice versa.

Substituents when present on any phenyl or heterocycl group may be the same or
25 different and include $R^a-(X)_n-$, (where R^a is as defined above, X is oxygen or sulfur and n is 0 or 1), optionally substituted amino, hydroxy, halogen, cyano, nitro, acyl, or two adjacent groups together with the carbon atoms to which they are attached can form an optionally substituted benzo or heterocyclic ring;

30 The term heterocycl includes both aromatic and non-aromatic heterocycl groups. Heterocycl groups are generally 5, 6 or 7-membered rings containing up to 4 hetero atoms selected from nitrogen, oxygen and sulfur. Examples of heterocycl groups are furyl, thienyl, pyrrolyl, pyrrolinyl, pyrrolidinyl, imidazolyl, dioxolanyl, oxazolyl, thiazolyl, imidazolyl, imidazolinyl, imidazolidinyl, pyrazolyl, pyrazolinyl, pyrazolidinyl, isoxazolyl, 35 isothiazolyl, oxadiazolyl, triazolyl, thiadiazolyl, pyranyl, pyridyl, piperidinyl, dioxanyl,

isothiazolyl, oxadiazolyl, triazolyl, thiadiazolyl, pyranyl, pyridyl, piperidinyl, dioxanyl, morpholino, dithianyl, thiomorpholino, pyridazinyl, pyrimidinyl, pyrazinyl, piperazinyl, triazinyl, thiazolinyl, benzimidazolyl, tetrazolyl, benzoxazolyl, imidazopyridinyl, 1,3-benzoxazinyl, 1,3-benzothiazinyl, oxazolopyridinyl, benzofuranyl, quinolinyl, 5 quinazolinyl, quinoxaliny, sulfolanyl, dihydroquinazolinyl, benzothiazolyl, phthalimido, benzofuranyl, azepinyl, oxazepinyl, thiazepinyl, tetrahydrofuryl, diazepinyl and benzodiazepinyl.

Amino groups may be substituted for example by one or two R¹ groups, or two 10 substituents can form a ring, preferably a 5 to 7-membered ring, which may be substituted and may contain other heteroatoms, for example morpholine, thiomorpholine, or piperidine. This ring can be substituted as for heterocyclyl.

The term acyl includes the residue of sulfur and phosphorus-containing acids as well 15 as carboxylic acids. Examples of acyl groups are thus -COR⁵, -COOR⁵, -CXNR⁵R⁶, -CON(R⁵)OR⁶, -COONR⁵R⁶, -CON(R⁵)NR⁶R⁷, -COSR⁵, -CSSR⁵, -S(O)_pR⁵, -S(O)₂OR⁵, -S(O)_pNR⁵R⁶, -P(=X)(OR⁵)(OR⁶), -CO-COOR⁵, where R⁵, R⁶ and R⁷, which may be the same or different, are hydrogen, optionally substituted alkyl, 20 optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted phenyl or optionally substituted heterocyclyl, or R⁵ and R⁶, or R⁶ and R⁷, together with the atom(s) to which they are attached can form a ring, p is 1 or 2 and X is O or S.

We have found that compounds of the invention wherein Z is oxygen are particularly 25 effective in combating fungi.

Preferred R¹ groups are hydrogen, 2-oxotetrahydrofuryl or optionally substituted alkyl. In particular when R¹ is optionally substituted alkyl we have found C₁-C₅ alkyl groups, e.g. methyl, to be especially preferred. Preferred substituents are 30 alkoxy carbonyl, alkanoyloxy, cyano and phenyl, itself optionally substituted by alkyl, alkoxy, haloalkyl or halogen.

R² is preferably hydrogen or alkyl, especially C₁-C₅ alkyl, e.g. methyl.

R³ and R⁴ can be the same or different and are preferably hydrogen, halogen or optionally substituted alkyl. It is generally desirable that one of R³ and R⁴ is halogen, especially bromine or chlorine, and particularly bromine, and the other is hydrogen. In particular when R³ or R⁴ is optionally substituted alkyl, we have found C₁-C₅ alkyl groups, especially tert.-butyl, to be most active. When R³ or R⁴ is substituted alkyl, preferred substituents are halogen, e.g. trifluoromethyl.

Although good activity has been shown for each fused ring system, generally the thieno[3,2-d]pyrimidine ring system is preferred.

10

The compounds of the invention have activity as fungicides, especially against fungal diseases of plants, e.g. mildews and particularly cereal powdery mildew (*Erysiphe graminis*) and vine downy mildew (*Plasmopara viticola*), rice blast (*Pynicularia oryzae*), cereal eyespot (*Pseudocercospora herpotrichoides*), rice sheath blight (*Pellicularia sasaki*), grey mould (*Botrytis cinerea*), damping off (*Rhizoctonia solani*), wheat brown rust (*Puccinia recondita*), late tomato or potato blight (*Phytophthora infestans*), apple scab (*Venturia inaequalis*), glume blotch (*Leptosphaeria nodorum*). Other fungi against which the compounds may be active include other powdery mildews, other rusts, and general pathogens of Deuteromycete, Ascomycete, Phycomycete and 20 Basidiomycete origin.

The invention thus also provides a method of combating fungi at a locus infested or liable to be infested therewith, which comprises applying to the locus a compound of formula I.

25

The invention also provides an agricultural composition comprising a compound of formula I in admixture with an agriculturally acceptable diluent or carrier.

30

The composition of the invention may of course include more than one compound of the invention.

In addition the composition can comprise one or more additional active ingredients, for example compounds known to possess plant-growth regulant, herbicidal,

fungicidal, insecticidal or acaricidal properties. Alternatively the compound of the invention can be used in sequence with the other active ingredient.

- The diluent or carrier in the composition of the invention can be a solid or a liquid
- 5 optionally in association with a surface-active agent, for example a dispersing agent, emulsifying agent or wetting agent. Suitable surface-active agents include anionic compounds such as a carboxylate, for example a metal carboxylate of a long chain fatty acid; an N-acylsarcosinate; mono- or di-esters of phosphoric acid with fatty alcohol ethoxylates or salts of such esters; fatty alcohol sulfates such as sodium dodecyl sulfate, sodium octadecyl sulfate or sodium cetyl sulfate; ethoxylated fatty alcohol sulfates; ethoxylated alkylphenol sulfates; lignin sulfonates; petroleum sulfonates; alkyl-aryl sulfonates such as alkyl-benzene sulfonates or lower alkylnaphthalene sulfonates, e.g. butyl-naphthalene sulfonate; salts of sulfonated naphthalene-formaldehyde condensates; salts of sulfonated phenol-formaldehyde condensates; or more complex sulfonates such as the amide sulfonates, e.g. the sulfonated condensation product of oleic acid and N-methyl taurine or the dialkyl sulfosuccinates, e.g. the sodium sulfonate of dioctyl succinate. Nonionic agents include condensation products of fatty acid esters, fatty alcohols, fatty acid amides or fatty-alkyl- or alkenyl-substituted phenols with ethylene oxide, fatty esters of
- 10 polyhydric alcohol ethers, e.g. sorbitan fatty acid esters, condensation products of such esters with ethylene oxide, e.g. polyoxyethylene sorbitan fatty acid esters, block copolymers of ethylene oxide and propylene oxide, acetylenic glycols such as 2,4,7,9-tetramethyl-5-decyne-4,7-diol, or ethoxylated acetylenic glycols.
- 15 Examples of a cationic surface-active agent include, for instance, an aliphatic mono-, di-, or polyamine as an acetate, naphthenate or oleate; an oxygen-containing amine such as an amine oxide or polyoxyethylene alkylamine; an amide-linked amine prepared by the condensation of a carboxylic acid with a di- or polyamine; or a quaternary ammonium salt.
- 20
- 25
- 30 The compositions of the invention can take any form known in the art for the formulation of agrochemicals, for example, a solution, a dispersion, an aqueous emulsion, a dusting powder, a seed dressing, a fumigant, a smoke, a dispersible powder, an emulsifiable concentrate or granules. Moreover it can be in a suitable

form for direct application or as a concentrate or primary composition which requires dilution with a suitable quantity of water or other diluent before application.

An emulsifiable concentrate comprises a compound of the invention dissolved in a

- 5 water-immiscible solvent which is formed into an emulsion with water in the presence of an emulsifying agent.

A dusting powder comprises a compound of the invention intimately mixed and ground with a solid pulverulent diluent, for example, kaolin.

10

A granular solid comprises a compound of the invention associated with similar diluents to those which may be employed in dusting powders, but the mixture is granulated by known methods. Alternatively it comprises the active ingredient absorbed or adsorbed on a pre-granular diluent, for example, Fuller's earth,

- 15 attapulgite or limestone grit.

Wettable powders, granules or grains usually comprise the active ingredient in admixture with a suitable surfactant and an inert powder diluent such as china clay.

- 20 Another suitable concentrate is a flowable suspension concentrate which is formed by grinding the compound with water or other liquid, a wetting agent and a suspending agent.

The concentration of the active ingredient in the composition of the present invention, as applied to plants is preferably within the range of 0.0001 to 1.0 per cent by weight, especially 0.0001 to 0.01 per cent by weight. In a primary composition, the amount of active ingredient can vary widely and can be, for example, from 5 to 95 per cent by weight of the composition.

- 30 In the method of the invention the compound is generally applied to seeds, plants or their habitat. Thus, the compound can be applied directly to the soil before, at or after drilling so that the presence of active compound in the soil can control the growth of fungi which may attack seeds. When the soil is treated directly the active compound can be applied in any manner which allows it to be intimately mixed with the soil such as by spraying, by broadcasting a solid form of granules, or by applying

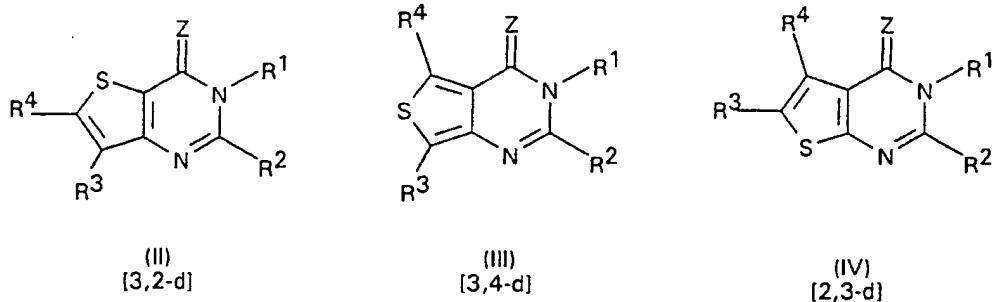
the active ingredient at the same time as drilling by inserting it in the same drill as the seeds. A suitable application rate is within the range of from 5 to 1000 g per hectare, more preferably from 10 to 500 g per hectare.

- 5 Alternatively the active compound can be applied directly to the plant by, for example, spraying or dusting either at the time when the fungus has begun to appear on the plant or before the appearance of fungus as a protective measure. In both such cases the preferred mode of application is by foliar spraying. It is generally important to obtain good control of fungi in the early stages of plant growth as this is the time
- 10 when the plant can be most severely damaged. The spray or dust can conveniently contain a pre- or post-emergence herbicide if this is thought necessary. Sometimes, it is practicable to treat the roots of a plant before or during planting, for example, by dipping the roots in a suitable liquid or solid composition. When the active compound is applied directly to the plant a suitable rate of application is from 0.025 to 5 kg per
- 15 hectare, preferably from 0.05 to 1 kg per hectare.

In addition, the compounds of the invention can be applied to plants, or parts thereof, which have been genetically modified to exhibit a trait such as fungal and/or herbicidal resistance.

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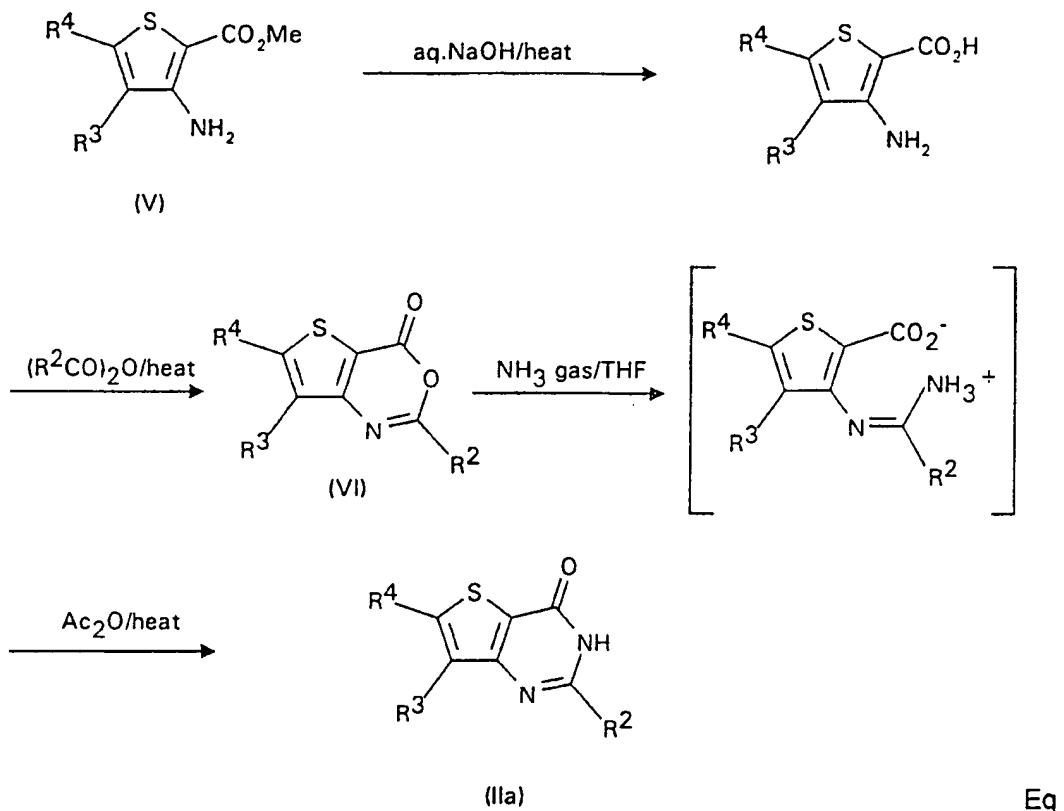
The general formula I covers thieno[3,2-d]pyrimidine derivatives II, thieno[3,4-d]pyrimidine derivatives III, and thieno[2,3-d]pyrimidine derivatives IV.



- Compounds of formula IIa, i.e. compounds of general formula II where R¹ is hydrogen and Z is oxygen, but R² is not hydrogen, may be prepared from compounds of formula V according to reaction Scheme 1. Compounds of formula V may be prepared by a number of methods; see for example references and reviews in Comprehensive Heterocyclic Chemistry, Eds Katritzky AR and Rees C W, (4), 863-

934 and Comprehensive Heterocyclic Chemistry II, Eds Katritzky A R, Rees C W and Scriven E F V, (2) 607-678.

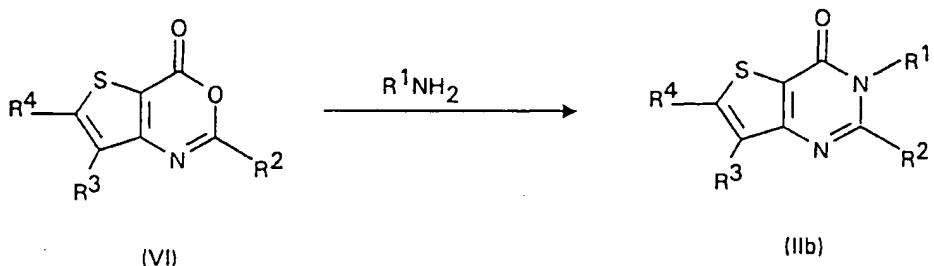
Scheme 1



- 5 Equivalent compounds of general formula III and IV can be made *mutatis mutandis* in similar manner.

- Compounds of formula IIb, i.e. compounds of formula II where Z is oxygen and R^2 is not hydrogen, can be prepared directly from intermediate VI in Scheme 1 by reaction 10 with R^1NH_2 (See Scheme 2).

Scheme 2

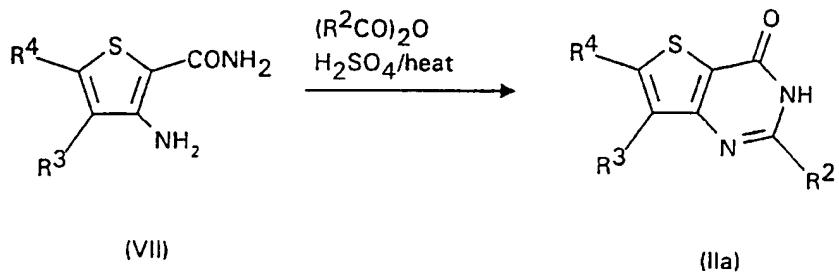


Equivalent compounds of general formula III and IV can be made *mutatis mutandis* in similar manner.

Compounds of formula IIa can be prepared from compounds of formula VII and acid anhydride. Preferred reaction conditions comprise heating VII and acetic anhydride in the presence of sulfuric acid according to reaction Scheme 3. Compounds of formula VII may be prepared according to methods disclosed by Klemm L H, Wang J.

- 5 Hawkins L, Journal of Heterocyclic Chemistry 32 (1995) 1039-1041.

Scheme 3

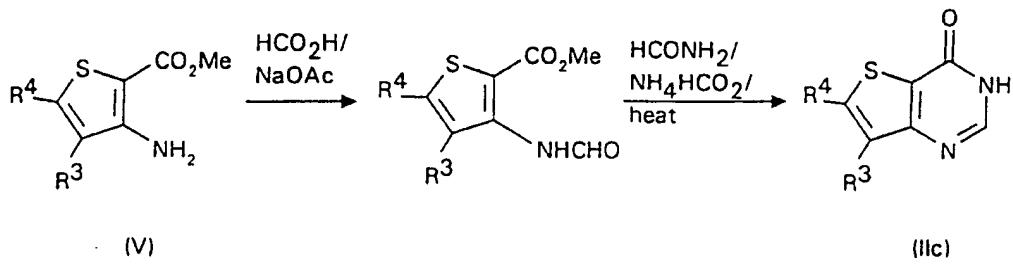


Equivalent compounds of general formula III and IV can be made *mutatis mutandis* in similar manner.

- 10

Compounds of formula IIc, i.e. compounds of general formula II where R¹ and R² are hydrogen and Z is oxygen, can be prepared from compound V in two steps according to reaction Scheme 4.

Scheme 4



- 15

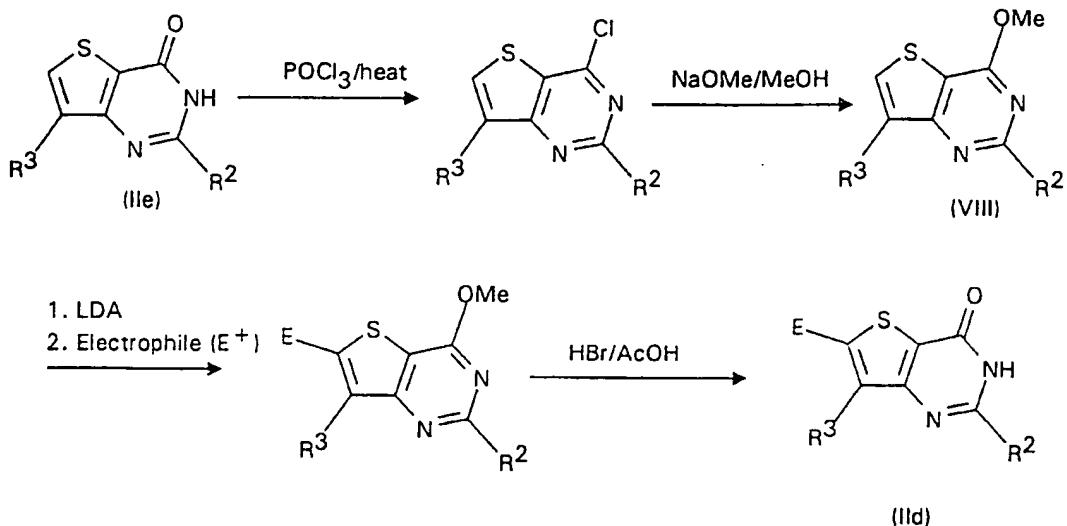
Equivalent compounds of general formula III and IV can be made *mutatis mutandis* in similar manner.

Compounds of formula II^d, i.e. compounds of general formula II where R¹ is

- 20 hydrogen, Z is oxygen, R² and R³ are groups inert to lithium diisopropylamide and R⁴
is a substituent E, can be prepared in four steps from Ile according to reaction
Scheme 5 wherein E is introduced using electrophilic substitution. Reaction conditions
for introducing substituent E involve treatment of intermediate VIII with lithium
diisopropylamide followed by addition of a suitable electrophile source. For example
25 when E is -CH(R)OH, CN, bromine or methyl, the electrophile source is respectively,

RC(=O)H , tosyl cyanide, *N*-bromosuccinimide or methyl iodide. When the group E is CH(R)OH , elimination of water may occur to form the corresponding compound II where E is alkenyl.

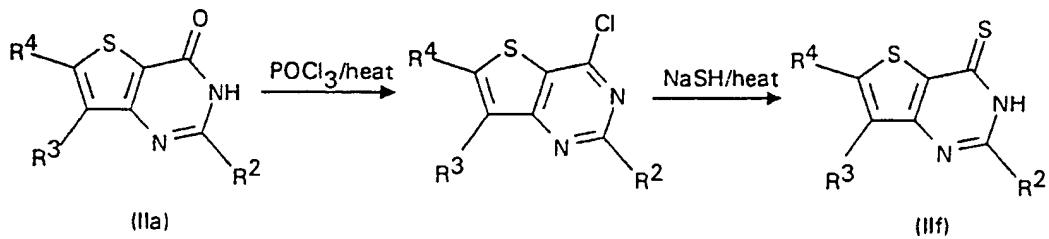
Scheme 5



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Compounds of formula II^f, i.e. compounds of formula II where R^1 is hydrogen and Z is sulfur can, be made in two steps from II^a, by reaction with phosphorus oxychloride followed by treatment with sodium hydrosulfide according to reaction Scheme 6.

Scheme 6



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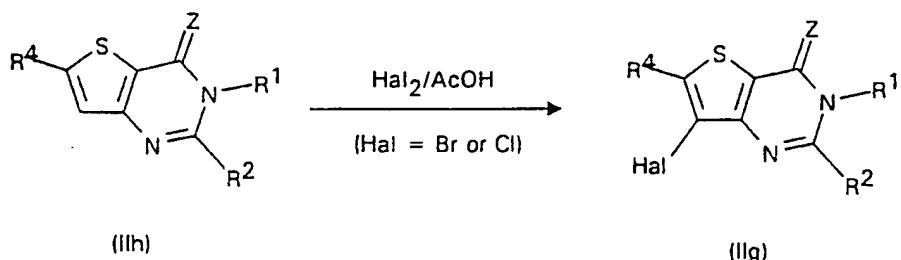
(IIIa)

(IIIf)

Equivalent compounds of general formula III and IV can be made *mutatis mutandis* in similar manner.

Compounds of formula II^g, i.e. compounds of general formula II where R^3 is a halogen, can be prepared according to reaction Scheme 7. When the halogen is bromine or chlorine, preferred reaction conditions comprise reacting II^h with bromine or chlorine in glacial acetic acid.

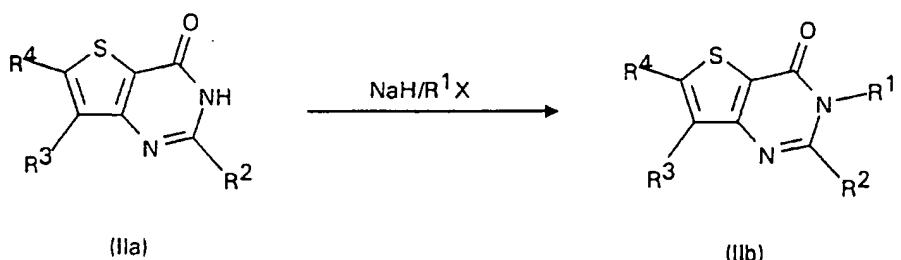
Scheme 7



Compounds of formula IIb, i.e. compounds of formula II where Z is oxygen, can be

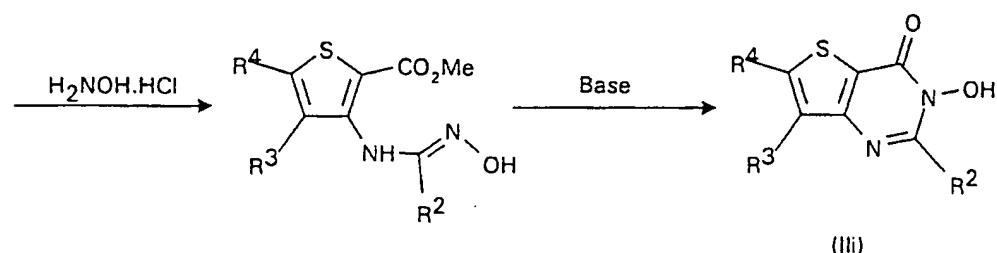
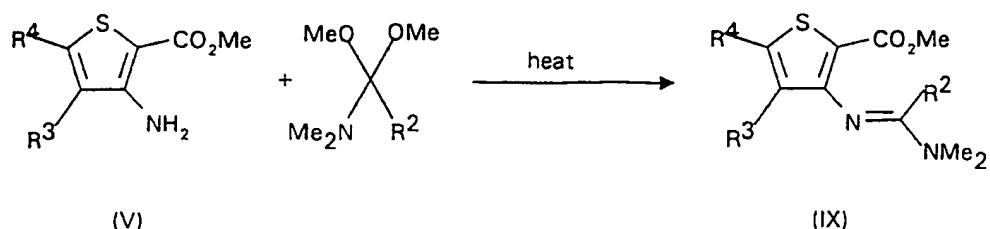
- 5 prepared from compounds of formula IIa, i.e. compounds of formula II where Z is oxygen and R¹ is hydrogen, by reacting IIa with base followed by treatment with R¹X where X is a leaving group. For example when R¹ is alkyl, preferred reaction conditions comprise treating IIa with sodium hydride followed by an alkyl iodide (Scheme 8).

10 Scheme 8



Equivalent compounds of general formula III and IV can be made *mutatis mutandis* in similar manner.

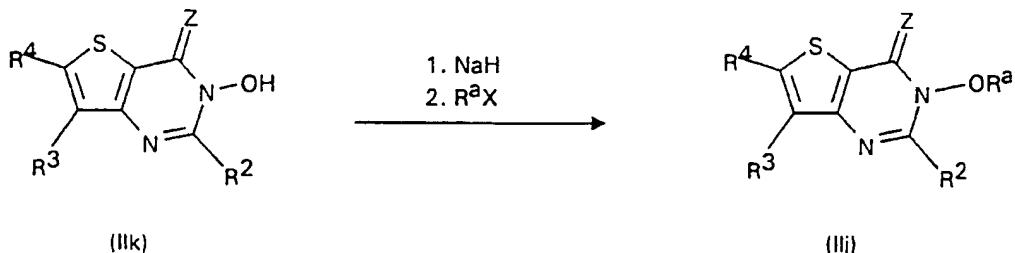
- 15 Compounds of formula III, i.e. compounds of formula II where R¹ is hydroxy and Z is oxygen, may be prepared in three steps starting from compound V according to reaction Scheme 9.

Scheme 9

Equivalent compounds of general formula III and IV can be made *mutatis mutandis* in similar manner.

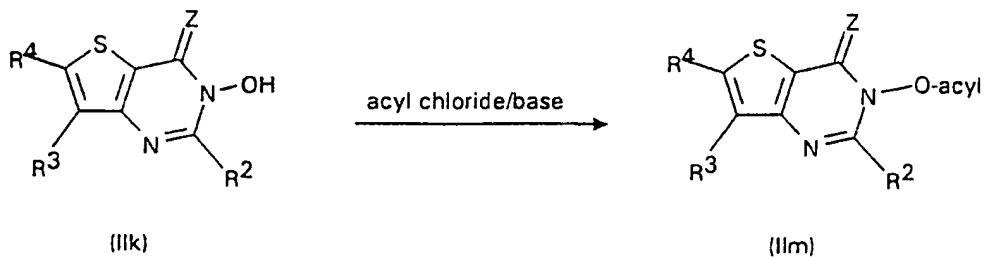
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Compounds of formula IIj, i.e. compounds of formula II where R¹ is R^aO, may be prepared according to Scheme 10 by reacting compounds of formula IIk with a suitable base, preferably sodium hydride followed by R^aX, where X is a leaving group.

10 Scheme 10

Equivalent compounds of general formula III and IV can be made *mutatis mutandis* in similar manner.

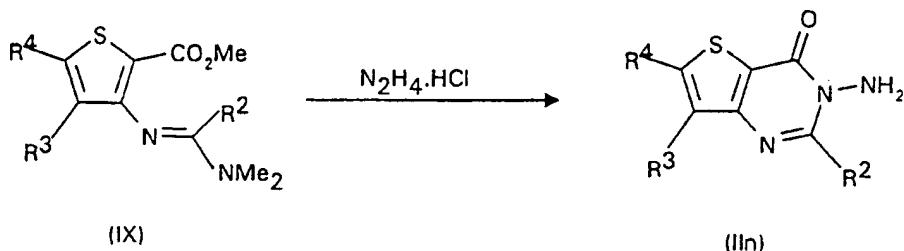
- 15 Compounds of formula IIm, i.e. compounds of formula II where R¹ is acyloxy, may be prepared according to Scheme 11 by reacting compounds of formula IIk with the corresponding acyl chloride.

Scheme 11

Equivalent compounds of general formula III and IV can be made *mutatis mutandis* in similar manner.

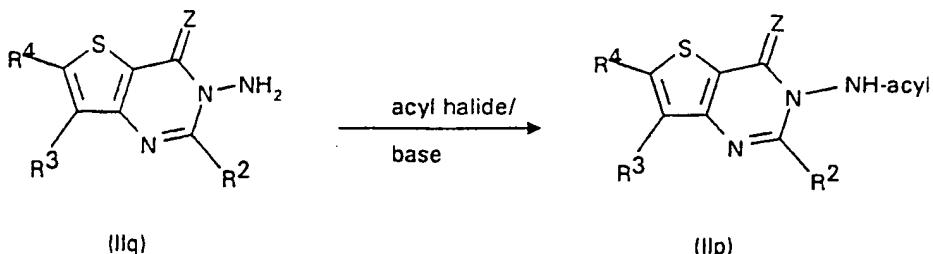
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Compounds of formula IIIn, i.e. compounds of general formula II where R¹ is NH₂ and Z is oxygen, can be prepared by reacting compounds of formula IX with hydrazine hydrochloride according to reaction Scheme 12. See Scheme 9 for the preparation of IX.

10 Scheme 12

Equivalent compounds of general formula III and IV can be made *mutatis mutandis* in similar manner.

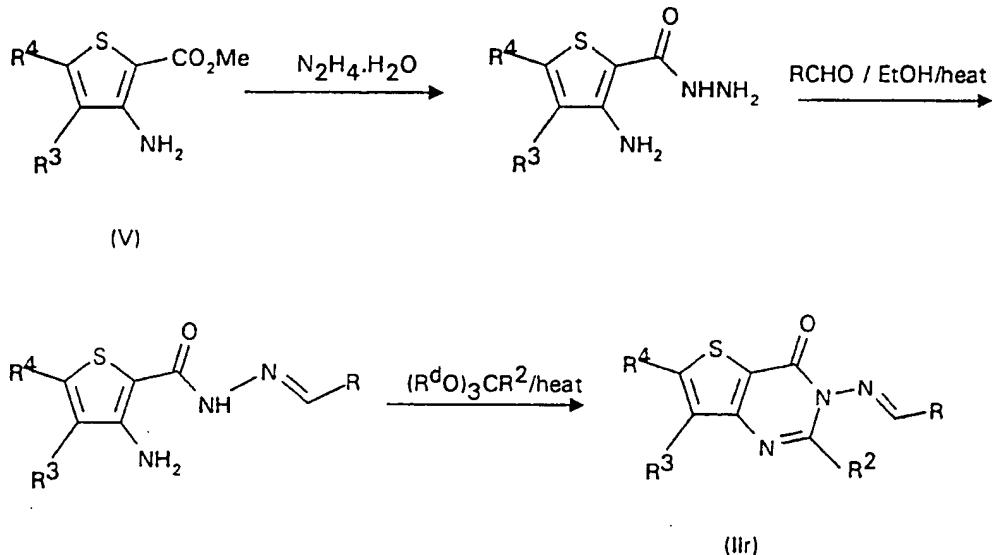
15 Compounds of formula IIp, i.e. compounds of general formula II where R¹ is NH-acyl, can be prepared by reacting compounds of formula IIq with the corresponding acyl halide according to reaction Scheme 13.

Scheme 13

20 Equivalent compounds of general formula III and IV can be made *mutatis mutandis* in similar manner.

Compounds of formula IIr, i.e. compounds of general formula II where R¹ is -N=CHR, R² is hydrogen and Z is oxygen, can be prepared according to reaction Scheme 14. R is preferably an aromatic group and R^d is preferably a lower alkyl group.

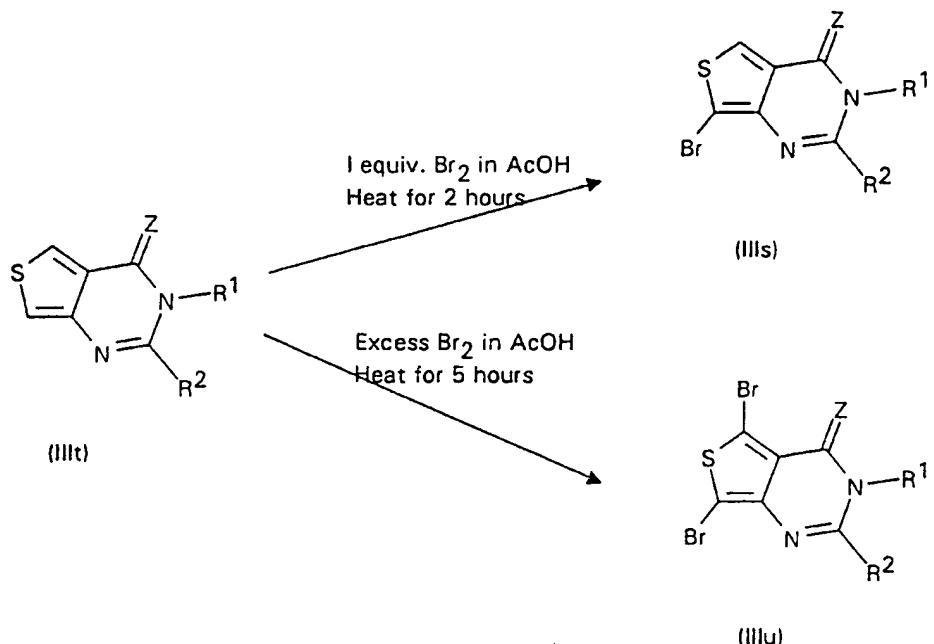
5 Scheme 14



Equivalent compounds of general formula III and IV can be made *mutatis mutandis* in similar manner.

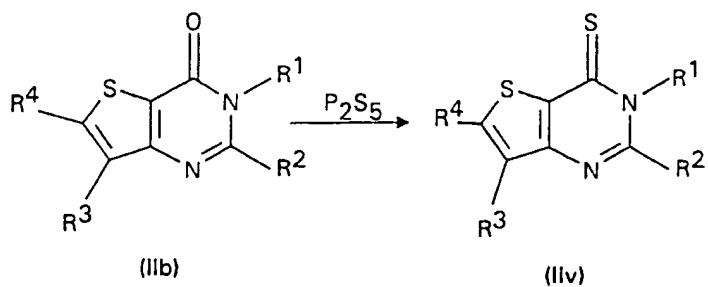
- 10 Compounds of IIIs, i.e. compounds of general formula III where R³ is bromine, can be prepared by treating compound of formula IIIt with bromine in glacial acetic acid heated under reflux for 2 hours. Continued heating for 5 hours gives the dibrominated compound IIlu, where R³ and R⁴ are both bromine (Scheme 15).

Scheme 15



Compounds of general formula IIb, i.e. compounds of formula II where Z is oxygen, can be converted to the corresponding compounds IIv where Z is sulfur by reaction with P₂S₅. The reaction is shown in Scheme 16.

Scheme 16



Equivalent compounds of general formula III and IV can be made *mutatis mutandis* in similar manner.

Other methods will be apparent to the chemist skilled in the art as will be the methods for preparing starting materials and intermediates.

15 The invention is illustrated in the following Examples. Structures of isolated novel compounds were confirmed by NMR and/or other appropriate analyses.

Example 17-Bromo-2-methyl-3,4-dihydrothieno[3,2-d]pyrimidin-4-one (compound 14a)

To a solution of the product from step b) (200 mg) in tetrahydrofuran (20 ml) was bubbled ammonia gas for 30 minutes at room temperature. The solvent was

- 5 removed to give a white solid which was dissolved in acetic anhydride (10 ml) and the solution was heated under reflux for 2 hours. The reaction mixture was allowed to cool and evaporated to dryness. The residue was taken up into water and the mixture filtered to give a solid which was dried to give the title product, m.p. 271-273 °C.

10

Preparation of starting materials

a) 3-Amino-4-bromo-2-thenoic acid

- A mixture of methyl 3-amino-4-bromo-2-thenoate (5 g) (for preparation see J. Gen. Chem. USSR, (1964), 34, 961), aqueous sodium hydroxide solution (2.1 ml of a 46% w/v solution) and water (19 ml) was heated under reflux for 2 hours. After cooling the reaction mixture was acidified with concentrated hydrochloric acid. The mixture was filtered and the resulting solid was washed with water then light petroleum (b.p. 60-80 °C) and then dried to give the title product.

20

b) 7-bromo-2-methylthieno[3,2-d]1,3-oxazin-4-one

- A solution of the product from step a) (3 g) in acetic anhydride (35 ml) was heated under reflux for 6 hours. On cooling the acetic anhydride was removed by evaporation and the solid dissolved in water and ethyl acetate. The aqueous layer was separated from the organic layer, and the organic layer dried (MgSO_4) and filtered. Removal of the solvent gave the title product.

Example 2

30 2-Methyl-3,4-dihydrothieno[3,2-d]pyrimidin-4-one (compound 7a)

A solution of 3-amino-2-thenamide (0.5 g) (for preparation see Klemm L H, Wang J, Hawkins L, Journal of Heterocyclic Chemistry 32 (1995) 1039-1041) and concentrated sulphuric acid (3 drops) in acetic anhydride (5 ml) was heated under reflux for 3½ hours. On cooling the solution was poured into water and extracted

with dichloromethane (x 3). The combined organic extracts were washed with water and dried ($MgSO_4$). Filtration and evaporation gave a residue which was purified by silica gel chromatography eluting with ethyl acetate to give the title product, m.p. 236-238 °C.

5

Example 3

6-Bromo-3,4-dihydrothieno[3,2-d]pyrimidin-4-one (compound 8a)

A solution of the product from step c) (0.22 g), hydrobromic acid (2 ml, 46% solution) in glacial acetic acid (10 ml) was heated under reflux for 6 hours. On 10 cooling the mixture was diluted with water and the mixture filtered. The solid was washed with water and air-dried to give the title product, m.p. 238-240 °C.

Preparation of starting materials

a) 4-Chlorothieno[3,2-d]pyrimidine

15 A mixture of compound 1h (see Table H) (10 g) and phosphorous oxychloride (100 ml) was heated under reflux for 5 hours. On cooling the solution was evaporated to dryness and the residue added to ice-water (with caution). The mixture was extracted with ethyl acetate and then with dichloromethane. The organic portions were washed with sodium 20 hydrogen carbonate solution followed by brine, dried ($MgSO_4$) and filtered through a silica pad. The filtrate was evaporated to give the title product.

b) 4-Methoxythieno[3,2-d]pyrimidine

25 To a suspension of sodium hydride (2 g 60% in oil) in dry dioxane (80 ml) at room temperature was added methanol (6 ml). When effervescence had subsided the product from step a) (5 g) was added and the reaction mixture stirred overnight at room temperature. The mixture was poured into water and extracted with ethyl acetate (x 3). The combined organic extracts were washed with brine, dried ($MgSO_4$), filtered and the solvent removed 30 to give the title product, m.p. 92-94 °C.

c) 6-Bromo-4-methoxythieno[3,2-d]pyrimidine

To a solution of the product from step b) (0.5 g) in dry tetrahydrofuran (20 ml) was added lithium diisopropylamide (1.53 ml, 2 M) at -78°C and stirring continued for 45 minutes. A solution of *N*-bromosuccinimide (0.6 g) in dry tetrahydrofuran (10 ml) was added dropwise at -78°C and then allowed to attain room temperature over one hour. The reaction mixture was poured into ice-water and extracted with ethyl acetate (x 3). The organic extracts were washed with brine, dried (MgSO_4), filtered and the solvent removed. The resulting solid was purified by silica gel chromatography eluting with light petroleum (60-80°C)/ethyl acetate (2:1) to give the title product, m.p. 111-113°C.

Example 47-Bromo-6-methyl-3,4-dihydrothieno[3,2-d]pyrimidin-4-one (compound 18a)

A stirred solution of compound 17a (see Table A) (2.1 g), bromine (0.2 ml) and glacial acetic acid (2 ml) was heated under reflux for 5 hours. On cooling, the reaction mixture was poured into water. The mixture was then filtered to give a solid which was washed with water and then light petroleum (b.p. 60-80 °C) and dried to give the title product, m.p. 320-322 °C.

20

The following compounds of formula IIa in Table A, i.e. compounds of formula II where Z is oxygen and R¹ is hydrogen, may be prepared by one or more methods analogous to those of Examples 1 to 4.

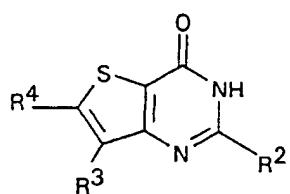


Table A

Cmp	R ²	R ³	R ⁴	m.p./°C
1a	H	Br	H	330-332
2a	H	NO ₂	H	238-240
3a	H	Cl	H	298-301
4a	H	Cl	Cl	278-289
5a	H	Br	Ph	329-331
6a	H	Br	tBu	299-301
7a	Me	H	H	236-238
8a	H	H	Br	238-240
9a	Ph	Br	H	292-294
10a	H	Me	Br	246-249
11a	Ph	H	H	276-278
12a	H	Br	Me ₃ Si	293-296
13a	Ph	Br	Br	341-343
14a	Me	Br	H	271-273
15a	Et	Br	H	290-292
16a	H	H	vinyl	84-88
17a	H	H	Me	201-203
18a	H	Br	Me	320-322

Example 53,6-Dimethyl-3,4-dihydrothieno[3,2-d]pyrimidin-4-one (compound 82b)

To a stirred suspension of sodium hydride (0.05 g, 60% in oil) in dry N-methylpyrrolidinone (2 ml) at room temperature was added compound 17a (0.1 g)

- 5 and stirring continued for 15 minutes. Iodomethane (0.1 ml) was then added and stirring continued at room temperature overnight. Water was added and the mixture extracted with ethyl acetate (x3). The organic extracts were combined and dried (MgSO_4), filtered through a silica pad and the solvent removed. The residue was triturated with diisopropyl ether to give the title product, m.p. 188-190 °C.

10

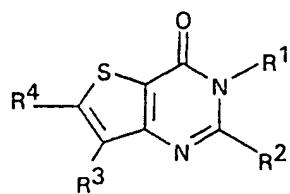
Example 67-Bromo-2-ethyl-3-(4-chlorobenzyl)-3,4-dihydrothieno[3,2-d]pyrimidin-4-one
(compound 70b)

- A stirred solution of the starting material (2.5 g), 4-chlorobenzylamine (1.43 g), p-toluenesulfonic acid (0.05 g) in xylene (135 ml) was heated at 138 °C for 3.5 hours. On cooling, the solvent was removed and the residue was triturated with diisopropyl ether, to give a solid which was washed and dried to give the title product, m.p. 97-99 °C.

20 Preparation of Starting Materials7-bromo-2-ethylthieno[3,2-d]1,3-oxazin-4-one

- A stirred solution of 3-amino-4-bromo-thenoic acid (5.0 g) and propionic anhydride (30 ml) was heated under reflux for 1 hour. Dilute sodium hydroxide solution was added and the mixture was extracted with ethyl acetate. The 25 organic extracts were combined and the solvent removed. The residue was dissolved in hot diisopropyl ether, filtered hot and cooled. On cooling the solution was filtered to give the title compound as a solid.

- The following compounds of formula II_s in Table B, i.e. compounds of formula II
30 where Z is oxygen may be prepared by one or more methods analogous to those of Examples 5 and 6.



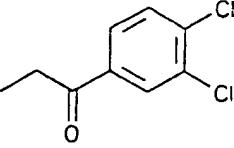
(IIIb)

Table B

Cmp	R ¹	R ²	R ³	R ⁴	m.p./°C
1b	Me	H	Br	H	212-214
2b	benzyl	H	Br	H	132-134
3b	allyl	H	Br	H	96-98
4b	iBu	H	Br	H	116-118
5b		H	Br	H	333-338
6b	iPr	H	Br	H	148-150
7b	3-PhO-benzyl	H	Br	H	117-120
8b	2-CF ₃ -benzyl	H	Br	H	137-139
9b	4-Cl-benzyl	H	Br	H	162-164
10b	2,6-diCl-benzyl	H	Br	H	181-183
11b	4-MeO-benzyl	H	Br	H	159-161
12b	propargyl	H	Br	H	144-146
13b	2,4,6-triCl-phenoxyethyl	H	Br	H	161-163
14b	-CH ₂ C(=O)OMe	H	Br	H	170-172
15b	-CH ₂ C(=O)OBu ₂	H	Br	H	169-171
16b	-CH ₂ C(=O)OH	H	Br	H	248-250
17b	Me	Me	H	H	126-127
18b	-CO ₂ Et	H	Br	H	126-128
19b	Ph	Me	Br	H	206-209
20b		H	Br	H	230-232

Cmp	R ¹	R ²	R ³	R ⁴	m.p./°C
21b	-CH ₂ (C=O)Ph	H	Br	H	195-196
22b	-CH ₂ CN	H	Br	H	199-201
23b	3,4-diCl-benzyl	H	Br	H	191-192
24b	2-Cl-benzyl	H	Br	H	127-131
25b	2,4-diCl-benzyl	H	Br	H	146-147
26b	Et	H	Br	H	156-159
27b	4-Br-benzyl	H	Br	H	170-175
28b	4-tBu-benzyl	H	Br	H	204-207
29b	2,4-diCl-benzyl	H	Me	H	158-159
30b	benzyl	H	Me	H	126-127
31b	2-CF ₃ -benzyl	H	Me	H	133-134
32b	3-PhO-benzyl	H	Me	H	98-99
33b	2-Cl-benzyl	H	Me	H	133-134
34b	4-Cl-benzyl	H	Me	H	169-170
35b		H	Me	H	224-225
36b	4-Br-benzyl	H	Me	H	166-167
37b	3,4-diMeO-benzyl	H	Me	H	136-137
38b	4-tBu-benzyl	H	Me	H	201-202
39b	2,4-diMe-benzyl	H	Br	H	124-126
40b	3,4-diMeO-benzyl	H	Br	H	190-193
41b		H	Br	H	201-206
42b		H	Br	H	196-200
43b	3-CF ₃ -benzyl	H	Br	H	150-152
44b	-(CH ₂) ₂ OC(=O)Me	H	Br	H	123-124
45b	-CH(Ph)-C(=O)OMe	H	Br	H	gum

Cmp	R ¹	R ²	R ³	R ⁴	m.p./°C
46b	-CH(CO ₂ Et) ₂	H	Br	H	92-93
47b	-CH(iPr)CO ₂ Et	H	Br	H	93-94
48b	-CH(Me)CO ₂ Et	H	Br	H	122-123
49b	-CH(Pr)CO ₂ Et	H	Br	H	82-84
50b		H	Br	H	248-250
51b	but-2-enyl	H	Br	H	133-134
52b	-CH ₂ C(=O)NH ₂	H	Br	H	277-281
53b	3-NO ₂ -benzyl	H	Br	H	216-218
54b	phenylpropyl	H	Br	H	81-83
55b	decyl	H	Br	H	50-52
56b	Et	Ph	H	H	121-123
57b	2,4-diCl-benzyl	H	Br	tBu	149-150
58b	2-CF ₃ -benzyl	H	Br	tBu	172-173
59b	3-PhO-benzyl	H	Br	tBu	123-124
60b	2-Cl-benzyl	H	Br	tBu	160-161
61b		H	Br	tBu	209-210
62b	4-Cl-benzyl	H	Br	tBu	116-117
63b	4-Br-benzyl	H	Br	tBu	121-122
64b	4-tBu-benzyl	H	Br	tBu	172-173
65b	benzyl	H	Br	tBu	oil
66b	3,4-diMeO-benzyl	H	Br	tBu	oil
67b	Me	H	Br	tBu	133-134
68b	Me	H	Br	Ph	202-204
69b	3-Cl-5-CF ₃ -2-pyridyl	H	Br	tBu	202-203
70b	4-Cl-benzyl	Et	Br	H	97-99
71b	Me	H	Me	H	194-195
72b	Me	Me	Br	H	222-224

Cmp	R ¹	R ²	R ³	R ⁴	m.p./°C
73b	Me	Et	Br	H	158-160
74b	2-NO ₂ -4-CF ₃ -phenyl	H	Br	H	212-214
75b	Me	H	-(CH) ₃ -N-		236-237
76b	3-Cl-5-CF ₃ -2-pyridyl	H	Br	H	180-183
77b	3-Ph-1,2,4-thia-diazol-5-yl	H	Br	H	270-272
78b	4-NO ₂ -phenyl	H	Br	H	285-290
79b	4-MeO-benzyl	Et	Br	H	114-116
80b	-CH ₂ CN	Et	Br	H	167-169
81b		Et	Br	H	194-196
82b	Me	H	H	Me	188-190
83b	Pr	Bu	Br	H	115-120
84b	Me	H	H	H	168-169

Example 77-Bromo-3-hydroxy-3,4-dihydrothieno[3,2-d]pyrimidin-4-one (compound 2c)

A solution of the starting material (1.4 g) and ethyldiisopropylamine (0.65 g) in

- 5 1,4-dioxan (20 ml) was heated under reflux for 24 hours. On cooling the reaction mixture was acidified with dilute hydrochloric acid and water (20 ml) was added. The solution was filtered to give a solid which was washed and dried to give the title product, m.p. 244-247 °C.

10 Preparation of Starting Materiala) Methyl 4-bromo-3-(dimethylaminomethylene)amino-2-thenoate

- A solution of methyl 3-amino-4-bromo-2-thenoic acid (for preparation see J. Gen. Chem. USSR, (1964), 34, 961) (5 g) and *N,N*-dimethylformamide dimethyl acetal (5 g) in toluene (30 ml) were heated under reflux for 8 hours. On cooling the solvent was removed and the residue purified by silica gel chromatography eluting with ethyl acetate : light petroleum (b.p. 60-80 °C) (1:3) to give the title compound.

b) Methyl 4-bromo-3-[(hydroxyiminomethyl)amino]-2-thenoate

To a stirred solution of the product from step a) (1.0 g) in methanol (10 ml) was added hydroxylamine hydrochloride (0.47 g) at room temperature.

5 After 10 minutes, stirring was stopped and the mixture allowed to stand at room temperature for 3 hours. The mixture was filtered to give a solid, which was washed with chilled methanol (3 ml) and dried to give the title product.

10 Example 8

7-Bromo-3-(4-methoxy)benzyloxy-3,4-dihydrothieno[3,2-d]pyrimidin-4-one
(compound 3c)

To a stirred suspension of sodium hydride (0.053 g, 60% in oil) in dry NMP (5 ml) at room temperature was added the product from Example 7 (0.325 g), and stirring was continued until effervescence ceased. 4-Methoxybenzyl chloride (0.2 g) was then added and the reaction mixture was stirred for 24 hours at room temperature. The reaction mixture was poured into water and the resulting white precipitate was filtered to give a white solid. This white solid was dissolved in dichloromethane and dried (MgSO_4). Removal of the solvent gave the title product, m.p. 178-180 °C.

20

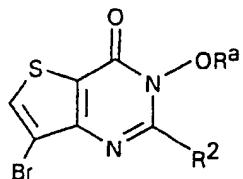
Example 9

3-Acetoxy-7-bromo-3,4-dihydrothieno[3,2-d]pyrimidin-4-one (compound 5c)

To a solution of acetyl chloride (0.234 g) in dry tetrahydrofuran (3 ml) was added a solution of the product from Example 7 (0.741 g) in pyridine (0.237 g) and 25 N -methylpyrrolidone (5 ml) at room temperature. The solution was stirred at room temperature for 3 days and then poured into water (15 ml). The resulting precipitate was filtered, washed with water and dried to give title product, m.p. 159-162 °C.

The following compounds of formula IIx in Table C, i.e. compounds of formula II

30 where Z is oxygen, R^1 is OR^a , R^3 is bromine and R^4 is hydrogen, may be prepared by methods analogous to those of Examples 7 to 9.



(IIx)

Table C

Cmp	R ^a	R ²	m.p./°C
1c	Me	H	152-154
2c	H	H	244-247
3c		H	178-180
4c	H	Me	216-220
5c	-C(=O)Me	H	159-162

Example 105 3-Amino-7-bromo-3,4-dihydrothieno[3,2-d]pyrimidin-4-one (compound 7d)

To a stirred solution of the product from step a) Example 7 (1.1 g) in methanol (7 ml) was added hydrazine hydrochloride (0.54 g) and stirring was continued for 1 hour. The reaction mixture was filtered to give a white solid which was washed with water and dried to give the title compound, m.p. 181-183 °C.

10

Example 11

3-Acetamido-7-bromo-3,4-dihydrothieno[3,2-d]pyrimidin-4-one (compound 9d)

To a stirred solution of acetyl chloride (0.16 g) in 1,4-dioxan (2 ml) was added a solution of the product from Example 10 (0.5 g) in pyridine (0.16 g) and *N*-methylpyrrolidinone (0.5 ml) and stirring was continued for 1 hour at room temperature. Water was added and the mixture was filtered to give a solid which was dried to give the title product, m.p. 273 °C.

Example 123-(4-Chlorobenzylidene)amino-7-methyl-3,4-dihydrothieno[3,2-d]pyrimidin-4-one
(compound 4d)

A solution of the product from step b (1.6 g), trimethyl orthoformate (10 ml), p-toluene sulfonic acid (catalytic) in xylene (100 ml) was heated under reflux for 2 hours. On cooling the reaction mixture was evaporated to dryness and recrystallised from toluene to give the title product, m.p. 213-215 °C.

Preparation of Starting Materials10 a) 3-Amino-4-methyl-2-thiophenecarbohydrazide

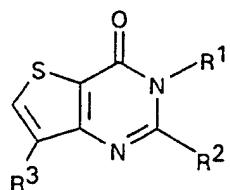
A solution of methyl 3-amino-4-methyl-2-thenoate (25 g) and hydrazine hydrate (20 ml) in butanol (150 ml) was heated under reflux for 18 hours. On cooling the solvent was removed and the residue was recrystallised from toluene to give the title product,

15 m.p. 141-143 °C.

b) N²-(4-chlorobenzylidene)-3-amino-4-methyl-2-thiophenecarbohydrazide

A solution of the product from step a) (3.4 g) and p-chlorobenzaldehyde (2.8 g) in ethanol (200 ml) was heated under reflux for 2 hours. On cooling the reaction mixture was filtered to give the title product.

The following compounds of formula IIy in Table D, i.e. compounds of formula II where Z is oxygen and R⁴ is hydrogen, may be prepared by one or methods analogous to those of Examples 10 to 12



(Ily)

Table D

Cmp	R ¹	R ²	R ³	m.p./°C
1d	NH ₂	4-Cl-phenyl	Me	175-7
2d		H	H	204-205
3d		Me	H	185-186
4d		H	Me	213-215
5d		H	Br	235-237
6d		Me	Br	242-245
7d	NH ₂	H	Br	181-183
8d	NH ₂	Me	Br	170-171
9d	-NHC(=O)Me	H	Br	273
10d	-N=CHOMe	H	H	120-122

Example 135 7-Bromo-3,4-dihydrothieno[3,2-d]pyrimidin-4-thione (compound 1e)

A solution of 7-bromo-4-chlorothieno[3,2-d]pyrimidine (see below for preparation) (2.0 g), sodium hydrosulfide hydrate (0.66 g) and *N*-methylpyrrolidinone (10 ml) was heated at 102 °C for 1 hour. Water (500 ml) and ethyl acetate (500 ml) were added and stirred for 1 hour. The layers were separated and the aqueous phase extracted with ethyl acetate (300 ml). The combined organic extracts were washed with brine (300 ml), dried ($MgSO_4$), treated with activated charcoal, then

filtered through a silica pad and the solvent removed to give the title product, m.p. 328 °C.

Preparation of starting materials

- 5 7-Bromo-4-chlorothieno[3,2-d]pyrimidine was prepared in analogous fashion to Example 3 step a), starting from compound 1a.

Example 14

3,4-Dihydrothieno[3,4-d]pyrimidin-4-one (compound 1f)

- 10 A stirred mixture of methyl 4-formamido-3-thenoate (see below) (3.39 g) and ammonium formate (3.4 g) in formamide (5 ml) was heated at 140 °C for 7 hours. On cooling, the mixture was poured into water, and the mixture filtered to give a solid which was washed with water followed by light petroleum (b.p. 60-80 °C) and air dried to give the title product, m.p. 275-278 °C.

15

Preparation of Starting Materials

Methyl 4-formamido-3-thenoate

A stirred solution of methyl 4-amino-3-thenoate (4 g), sodium acetate trihydrate (2.8 g) and formic acid (27 ml) was heated at 95 °C for 1 hour.

- 20 On cooling the solution was poured into water, and the solution filtered to give the title product as a solid.

Example 15

5,7-Dibromo-3,4-dihydrothieno[3,4-d]pyrimidin-4-one (compound 2f)

- 25 A solution of the product from Example 14 (0.9 g) and excess bromine (0.4 ml) in glacial acetic acid (100 ml) were heated at 100 °C for 5 hours until no bromine remained. On cooling the solvent was removed and the residue was dried. The residue was recrystallised from acetic acid to give the title product, m.p. >250 °C

30 Example 16

7-Bromo-3,4-dihydrothieno[3,4-d]pyrimidin-4-one (compound 3f)

A solution of the product from Example 14 (0.9 g) and bromine (0.3 ml) in glacial acetic acid (100 ml) were heated at 100 °C for 2 hours. On cooling the solvent

was removed and the residue was dried. The residue was recrystallised from acetic acid to give the title product, m.p. 226-229 °C.

Example 17

5 3,4-Dihydrothieno[2,3-d]pyrimidin-4-one (compound 5g)

The product from step b) (4.38 g) and ammonium formate (4.38 g) in formamide (18 ml) was heated with stirring at 150°C for 7 hours. The mixture was cooled and poured into water. The precipitated solid was filtered, washed with water followed by dichloromethane and dried to give the title product, m.p. 256-8°C.

10

Preparation of Starting Materials

a) Ethyl 2-amino-3-thenoate

Piperidine (20.7 ml) was added dropwise with stirring to a mixture of 2,5-dihydroxy-1,4-dithiane (17.5 g) and ethyl cyanoacetate (23.7 g). The mixture was stirred at room temperature for 4 hours and then allowed to stand overnight. It was filtered and the filtrate evaporated to dryness. The residue was dissolved in ether, filtered and evaporated to dryness. The residue was triturated with light petroleum (b.p. 60-80°C) containing a small amount of ethyl acetate. The gummy solid obtained was purified by silica gel column chromatography and the semi-solid product was triturated with water, filtered and washed with light petroleum (b.p. 60-80°C) and dried to give the title product.

b) Ethyl 2-formamido-3-thenoate

25 The product from step a) (14.6 g) was added to a mixture of acetic anhydride (24.3 ml) and formic acid (24.3 ml) with stirring and cooling. The mixture was stirred at room temperature for 4 hours and evaporated under reduced pressure. The residue was dissolved in ether and cooled in dry ice. The precipitate was filtered off and dried to give the title product.

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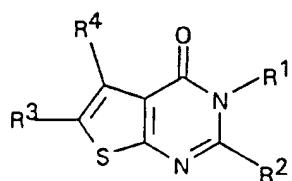
Example 18

6-Bromo-3,4-dihydrothieno[2,3-d]pyrimidin-4-one (compound 6g)

The product from Example 17 (0.75 g) was added to glacial acetic acid (10 ml) and heated with stirring until it dissolved. Bromine (0.75 ml) was then added and the mixture immediately set solid. More acetic acid was added and the mixture broken

up. It was then heated at 80°C for 6½ hours, cooled and poured into ice-water. The solid was filtered and washed with water followed by dichloromethane and dried to give the title product, m.p. 304°C.

- 5 The following compounds of formula IVz in Table G, i.e. compounds of formula IV where Z is oxygen, may be prepared by one or more methods analogous to those of Examples 5, 17 and 18.



(IVz)

10

Table G

Cmp	R ¹	R ²	R ³	R ⁴	m.p./°C
1g	H	H	H	Ph	
2g	H	CF ₃	-(CH ₂) ₄ -		
3g	H	Et	-(CH ₂) ₄ -	235-240	
4g	H	H	H	Me	235-237
5g	H	H	H	H	256-258
6g	H	H	Br	H	301-304
7g	H	H	H	2-thienyl	
8g	H	Me	-(CH ₂) ₃ -		
9g	H	H	Br	Me	241-243
10g	2,4-diCl-benzyl	H	H	Me	130-131
11g	Benzyl	H	H	Me	123-124
12g	2-CF ₃ -benzyl	H	H	Me	106-107
13g	2-Cl-benzyl	H	H	Me	124-125
14g	4-Cl-benzyl	H	H	Me	143-144

Cmp	R ¹	R ²	R ³	R ⁴	m.p./°C
15g		H	H	Me	180-181
16g	4-Br-benzyl	H	H	Me	155-156
17g	3,4-diMeO-benzyl	H	H	Me	161-162
18g	4-tBu-benzyl	H	H	Me	160-161
19g	3-PhO-benzyl	H	H	Me	oil
20g	H	H	Br	Ph	271-273
21g	Me	H	H	Me	132-133

The following compounds of formula IIa in Table H, i.e. compounds of formula II where Z is oxygen and R¹ is hydrogen, may be prepared by methods analogous to those of Example 17 replacing ethyl 2-amino-3-thenoate in step a) with the
5 corresponding 3-amino-2-thenoate.

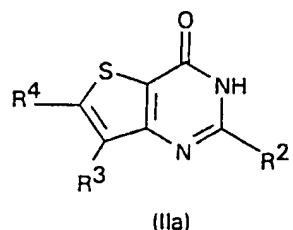


Table H

Cmp	R ²	R ³	R ⁴	m.p./°C
1h	H	H	H	228-230
2h	H	Me	H	243-246
3h	CCl ₃	H	H	230-234
4h	H	H	Ph	271-273
5h	H	H	TBu	235-237
6h	H	Ph	H	235-237
7h	H	H	4-Cl-phenyl	
8h	H	Ph	CF ₃	
9h	H	H	4-F-phenyl	
10h	H	-(CH ₂) ₃ N-		340-342

Test Example

Compounds were assessed for activity against one or more of the following:

Erysiphe graminis f sp. tritici: wheat powdery mildew

5 *Phytophthora infestans*: late tomato blight

Pyricularia oryzae: rice blast

Leptosphaeria nodorum: glume blotch

Plasmopara viticola: downy mildew of vines

10 Aqueous solutions or dispersions of the compounds at the desired concentration, including a wetting agent, were applied by spray or by drenching the stem base of the test plants, as appropriate. After a given time, plants or plant parts were inoculated with appropriate test pathogens and kept under controlled environmental conditions suitable for maintaining plant growth and development of the disease. After an appropriate time, the degree of infection of the affected part of the plant was visually estimated. Compounds are assessed on a score of 1 to 3 where 1 is little or no control, 2 is moderate control and 3 is good to total control. At a concentration of 500 ppm (w/v) or less, the following compounds scored 2 or more against the fungi specified.

20

Erysiphe graminis f sp. tritici

3a, 7a, 12a, 1b, 5b, 6b, 7b, 8b, 9b, 10b, 11b, 13b, 14b, 16b, 24b, 25b, 26b, 27b, 41b, 43b, 45b, 47b, 50b, 52b, 53b, 54b, 55b, 61b, 66b, 2f, 3f and 5g.

25 *Phytophthora infestans*

1a, 8a, 14b, 15b, 2d, 3f, 3h and 9h.

Pyricularia oryzae

1a, 3a, 4a, 6a, 7a, 8a, 9a, 10a, 12a, 14a, 1b, 4b, 5b, 6b, 7b, 8b, 9b, 10b, 11b,

30 18b, 20b, 21b, 22b, 25b, 26b, 27b, 30b, 40b, 41b, 43b, 44b, 45b, 46b, 47b, 48b, 49b, 50b, 51b, 52b, 54b, 55b, 57b, 63b, 65b, 66b, 2c, 2d, 3d, 7d, 1e, 4g, 5g, 6g, 9g, 17g, 18g, 19g, 1h, 2h and 3h.

Leptosphaeria nodorum

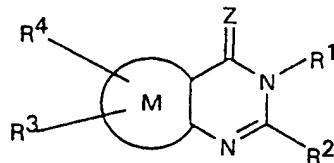
2b, 5b, 6b, 7b, 9b, 10b, 11b, 13b, 18b, 28b, 29b, 33b, 39b, 41b, 43b, 51b, 1f, 6g, 19g, 4h and 8h.

5 *Plasmopara viticola*

1b, 5b, 12b, 14b, 15b, 18b, 19b, 20b, 21b, 22b, 23b, 28b, 40b, 41b, 56b, 1f, 2f, 3f, 3g, 10g and 3h.

CLAIMS

1 The use in combating fungi of compounds of general formula I



(I)

wherein

- 5 R¹ is hydrogen, hydroxy, acyl, acyloxy, optionally substituted amino, R^a, R^a₃Si, R^aS or R^aO, where R^a is optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted aryl or optionally substituted heterocyclyl;
- 10 R² has the same meaning as R^a or can be hydrogen;
Z is oxygen or sulfur;
M is a thiophene ring; and
R³ and R⁴, which may be the same or different, have the same meaning as R^a or can be optionally substituted amino, hydrogen, halogen, cyano, nitro or a group OR^C or S(O)_mR^C, where R^C has the same meaning as R^a or is hydrogen or acyl and m is 0, 1 or 2; or R³ and R⁴ together with the atoms to which they are attached form an optionally substituted carbocyclic or heterocyclic ring;
together with tautomers of compounds where R¹ is hydrogen.
- 20 2 The use in combating fungi of compounds according to claim 1 wherein Z is oxygen.
- 25 3 The use in combating fungi of compounds according to claim 1 or 2 wherein R¹ is hydrogen, 2-oxotetrahydrofuryl or optionally substituted alkyl.
- 4 4 The use in combating fungi of compounds according to claim 3, wherein R¹ is hydrogen.

- 5 The use in combating fungi of compounds according to claim 3, wherein
R¹ is C₁-C₅-alkyl, optionally substituted by alkoxy carbonyl, alkanoyloxy, cyano
or phenyl, itself optionally substituted by alkyl, alkoxy, haloalkyl or halogen.
- 5
- 6 The use in combating fungi of compounds according to any preceding claim
wherein R² is hydrogen or alkyl.
- 7
- 7 The use in combating fungi of compounds according to any preceding claim
10 wherein R³ and R⁴, which may be the same or different, are hydrogen or
halogen.
- 8
- 8 The use in combating fungi of compounds according to any preceding claim
which compound is a thieno[3,2-d]pyrimidine derivative.
- 15
- 9 7-bromo-3-methyl-3,4-dihydrothieno[3,2-d]pyrimidin-4-one

INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 98/01286

A. CLASSIFICATION OF SUBJECT MATTER
 IPC 6 A01N43/90 C07D495/04

According to International Patent Classification(IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 A01N C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 97 02262 A (DU PONT :BEREZNAK JAMES FRANCIS (US); CHANG ZEN YU (US); STERNBERG) 23 January 1997 see claim 10 ---	1-3, 5, 7, 8
X, P	WO 97 33890 A (CIBA GEIGY AG ;WALTER HARALD (CH)) 18 September 1997 see claim 10 ---	1-3, 5, 7, 8
X	EP 0 665 224 A (NIPPON SODA CO) 2 August 1995 see claim 8 see table 2 -----	1-4, 7, 8

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

* Special categories of cited documents :

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- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 98/01286

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